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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/714,602	11/16/2000	David William Holden	RPMS 101 CON(3)	4552

23579 7590 11/17/2003

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EXAMINER

LEFFERS JR, GERALD G

ART UNIT	PAPER NUMBER
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1636

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DATE MAILED: 11/17/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

Application No.

09/714,602

Applicant(s)

HOLDEN, DAVID WILLIAM

Examiner

Gerald G Leffers Jr., PhD

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

1) ☒ Responsive to communication(s) filed on 30 April 2003.

2a) ☐ This action is FINAL.

2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

4) ☒ Claim(s) 3,57-73,76-78 and 86 is/are pending in the application.

4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.

5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.

6) ☒ Claim(s) 3,57-73,76-78 and 86 is/are rejected.

7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.

8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

## Priority under 35 U.S.C. §§ 119 and 120

12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some \* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.

2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.

3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

13) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

## Attachment(s)

1) ☐ Notice of References Cited (PTO-892)

2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 15.

4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_.

5) ☐ Notice of Informal Patent Application (PTO-152)

6) ☐ Other: \_\_\_\_\_.

### **DETAILED ACTION**

Upon further review of the instant application and its predecessors, it is apparent that the instant application comprises additional subject matter not contained within the applications to which priority is claimed under 35 U.S.C. 120 (i.e. applications 09/201,945 and 08/637,759) and, thus, the instant application is not a continuation of the prior applications. This fact has necessitated the following denial of priority to the cited applications for the claimed subject matter and objections to the specification and declaration/oath.

### ***Response to Amendment***

Receipt is acknowledged of an amendment, filed 2/7/03 as Paper No. 14, in which claims were cancelled (claims 74-75 and 79). Finally, receipt is also acknowledged of a set of Terminal Disclaimers for the pending claims over U.S. Patents 5,876,931; 6,342,215; & 6,015,969. These papers are proper and have been entered into the file. These papers have obviated the outstanding rejections of record for Obviousness Double Patenting.

Any other rejection of record not addressed herein is hereby withdrawn. This action is not final as there are new grounds of rejection made herein that were not necessitated by applicant's amendment of the claims in Paper No. 18.

Claims 3, 57-73, 76-78 and 86 are pending in the instant application.

### *Sequence Compliance*

Receipt is acknowledged of an amendment, filed 4/30/03 as Paper No. 18, in which the specification was amended to include sequence identifiers in the Brief Description of the Drawings for Figure 11. The application appears to now be in sequence compliance.

### *Priority*

Applicant has attempted to claim priority to applications 09/201,945 and 08/637,759 under 35 U.S.C. 120 as a continuation application of these prior applications. However, applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 120 as follows:

The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application); the disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994). There is no disclosure in the 09/201,945 or 08/637,759 applications of the broadly claimed methods recited in the pending claims.

The earlier applications were specifically limited to methods of identifying genes where the methods comprise insertional inactivation of genes within the genome of a target microorganism (e.g. a pathogen) with transposon elements (or "transposon-like" elements) comprising a unique nucleic acid tag sequence. In these methods, a plurality of mutants having unique tag sequences are introduced into a particular environment (e.g. a multicellular organism)

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and grown for some period of time. Surviving microorganisms are harvested from the particular environment and the unique nucleic acid “tags” obtained from the surviving microorganisms probed with a bank of the unique nucleic acid tags for all of the microorganisms introduced into the particular environment. Those tags from the bank of unique tags that do not hybridize with those present in the genomes of the surviving microorganisms correspond to insertion events into genes essential for viability of the microorganism in the particular environment. Thus, the methods result in the identification of microorganisms having a reduced adaptation to a particular environment.

The instant claims, on the other hand, recite methods that are not reliant upon insertional inactivation of genes by a transposon or “transposon-like” element, nor do they necessarily depend upon a comparison of the unique tag sequences isolated from surviving microorganism to those initially introduced into the particular environment (e.g. see claims 57 and 86). As such, the pending claims encompass embodiments that are not encompassed by the 09/201,945 or 08/637,759 applications.

This application repeats a substantial portion of prior Application No. 09/201,945, filed 12/1/1998, and adds and claims additional disclosure not presented in the prior application. Since this application names an inventor or inventors named in the prior application, it may constitute a continuation-in-part of the prior application. Should applicant desire to obtain the benefit of the filing date of the prior application, attention is directed to 35 U.S.C. 120 and 37 CFR 1.78.

***Specification***

The specification is objected to as failing to provide proper antecedent basis for the claimed subject matter. See 37 CFR 1.75(d)(1) and MPEP § 608.01(o). Correction of the following is required: there is no literal support in the originally filed specification for the broadly claimed methods recited in the pending claims for the reasons outlined above. Applicant submitted a preliminary amendment on the filing date of the instant application comprising the pending claims and recited subject matter. Therefore, the pending claims do not constitute new matter. It is necessary, however, for applicant to amend the instant specification to provide antecedent support for the subject matter recited in the pending claims. Care should be taken to limit what is incorporated into the specification to that which is recited in the claims submitted in the preliminary amendment submitted on 11/16/2000.

***Oath/Declaration***

The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because:

The specification to which the oath or declaration is directed has not been adequately identified. See MPEP § 601.01(a).

As indicated above, the instant application is not a continuation application of 09/201,945 due to the new subject matter introduced by the preliminary amendment filed on the filing date (11/16/2000). Therefore, applicant cannot rely upon a declaration filed for application 08/637,759, upon which application 09/201,945 was a continuation. It is necessary for applicant

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to submit a new declaration that addresses the new methodology introduced by the preliminary amendment filed 11/16/2000.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 3, 57-73, 76-78 and 86 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This is a new rejection.**

Each of the claims is drawn to a method of identifying a microorganism having a reduced adaptation to a particular environment comprising: (a) a plurality of microorganisms wherein each contains a different marker sequence; (b) introducing the plurality of microorganisms in a particular environment and allowing those that are able to grow in that environment to do so; (c) retrieving the ones that are able to grow from the particular environment; and (d) selecting an individual microorganism having a reduced capacity to proliferate in the particular environment by comparing any marker sequence in the nucleic acid present in the retrieved microorganisms to the original marker sequences put into the particular environment (e.g. claim 86). The microorganisms can be mutant microorganisms. The rejected claims encompass embodiments wherein the original microorganisms are not mutants, or are mutants generated by an undefined

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method, where the nature of the tag sequence is not defined. Nor is the nature of the marker sequence defined. The claims do not explicitly link the marker sequence obtained in step (c) to that originally present in the microorganism (see the 112 2<sup>nd</sup> rejection below). Thus, the rejected claims encompass a number of different sequence markers introduced into the microorganisms in different ways and used in different ways to determine the identity of a microorganism having a reduced capacity to adapt to a particular environment.

The instant specification is explicitly limited to methods of identifying genes where the methods comprise insertional inactivation of genes within the genome of a target microorganism (e.g. a pathogen) with transposon elements (or “transposon-like” elements) comprising a unique nucleic acid tag sequence. In these methods, a plurality of mutants having unique tag sequences are introduced into a particular environment (e.g. a multicellular organism) and grown for some period of time. Surviving microorganisms are harvested from the particular environment and the unique nucleic acid “tags” obtained from the surviving microorganisms probed with a bank of the unique nucleic acid tags for all of the microorganisms introduced into the particular environment. Those tags from the bank of unique tags that do not hybridize with those present in the genomes of the surviving microorganisms correspond to insertion events into genes essential for viability of the microorganism in the particular environment. Thus, the methods result in the identification of microorganisms having a reduced adaptation to a particular environment.

The specification does not describe any other approach for providing microorganisms, mutant or otherwise, having unique sequence tags or markers for use in the claimed methods. The specification describes no other means of “selecting by comparison” of microorganisms having a reduced ability to adapt to a particular environment than comparison of nucleic acid



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tags present within transposable elements from surviving microorganisms to those present in the microorganisms prior to their insertion into the particular environment. The specification does not provide *any* description of what other methods embraced by the claims might look like (i.e. what the methods steps would be). Therefore, the skilled artisan would not have been able to envision a sufficient number of different methods embraced by the rejected claims to describe the broadly claimed genus of such methods of identifying a microorganism have a reduced adaptation to a particular environment.

Claims 3, 57-73, 76-78 and 86 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for embodiments wherein (1) a plurality of microorganisms is provided wherein each of the microorganisms is independently mutated by the insertional inactivation of a gene with a nucleic acid comprising a unique marker sequence so that each mutant contains a different marker sequence, and (2) the mutant microorganism having a reduced ability to adapt to a particular environment is selected by (i) comparison of the different unique marker sequences obtained from microorganisms that are able to grow in the particular environment to the collection of unique marker sequences present in the plurality of microorganisms introduced into the particular environment, and (ii) the mutant microorganism is identified based upon its lack of a unique marker sequence obtained from the population of microorganisms able to grow in the particular environment, does not reasonably provide enablement for methods that do not comprise these elements. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. **This is a new rejection.**

Enablement is considered in view of the Wands factors (MPEP 2164.01(A)). These include: nature of the invention, breadth of the claims, guidance of the specification, the existence of working examples, state of the art, predictability of the art and the amount of experimentation necessary. All of the Wands factors have been considered with regard to the instant claims, with the most relevant factors discussed below.

*Nature of the invention:* The nature of the invention is complex, involving the identification of a microorganism having a reduced ability to thrive in a particular environment based upon a comparison of nucleic acid marker sequences in a population of surviving microorganisms to nucleic acid marker sequences present in the plurality of microorganisms introduced into a particular environment. In order to practice the invention, there needs to be some correlation between the marker sequences present in the microorganisms that survive compared to those initially introduced into the environment

*Breadth of the claims:* The breadth of the claims exacerbates the complexity of the invention due to the fact that the claims do not provide an explicit correlation between the nature of the different marker sequences present in the microorganisms and their survival in the particular environment. For this reason, the claims encompass embodiments that are not described or taught in the instant specification.

*Guidance of the specification/The existence of working examples:* The instant specification is explicitly limited to methods of identifying genes where the methods comprise insertional inactivation of genes within the genome of a target microorganism (e.g. a pathogen) with transposon elements (or “transposon-like” elements) comprising a unique nucleic acid tag sequence. In these methods, a plurality of mutants having unique tag sequences are introduced

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into a particular environment (e.g. a multicellular organism) and grown for some period of time. Surviving microorganisms are harvested from the particular environment and the unique nucleic acid “tags” obtained from the surviving microorganisms probed with a bank of the unique nucleic acid tags for all of the microorganisms introduced into the particular environment. Those tags from the bank of unique tags that do not hybridize with those present in the genomes of the surviving microorganisms correspond to insertion events into genes essential for viability of the microorganism in the particular environment. Thus, the methods result in the identification of microorganisms having a reduced adaptation to a particular environment.

The specification provides no description or teaching of any other approach to practicing the claimed methods. No other method is taught for correlating the presence of a marker sequence in the initial population of microorganisms with the lack of the same sequence in the surviving population to identification of microorganisms having a reduced adaptation to the particular environment.

*State of the art:* The prior art does not appear to anticipate or suggest the claimed methods at the time of filing. Therefore, the prior art does not appear to offset the deficiencies of the instant specification with regard to practicing the claimed methods without insertional inactivation of host cell genes and direct correlation of the unique nucleic acid marker sequences present in the survivors to those in the initial population of microorganisms introduced into the particular environment.

*Predictability of the art/Amount of Experimentation Required:* Given the lack of teachings in the instant specification and prior art concerning practicing the claimed methods in their full scope, it would have been unpredictable to attempt the claimed methods. One would

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have had to envision alternative methods for correlating the presence of particular marker sequences present in the surviving population of microorganisms with marker sequences present in the input population in order to identify microorganisms having a reduced capacity to adapt to the particular environment. If unsuccessful, which is likely given the lack of any alternative description or teaching from the prior art as to how to practice the claimed invention, one would have had to envision changes to the first approach, or an entirely new approach. Therefore, it would have taken undue, unpredictable experimentation in order to practice the claimed invention in the full, broad scope now claimed.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 3, 57-73, 76-78 and 86 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. **This is a new rejection.**

Claims 57 and 86 each recite a limitation is step (d) where an individual mutant having a reduced capacity to proliferate in the particular environment is selected by comparing “any” marker sequences present in the nucleic acid present in the retrieved microorganisms in step (c) to the different marker sequences of step (a). There is no clear and positive prior antecedent basis for the term “any marker sequences”, making it unclear how one is to practice the claimed invention if there is no correlation between the marker sequences present in the population initially put into the particular environment and those present in the survivors.

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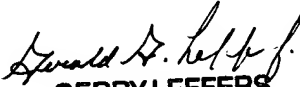
***Conclusion***

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gerald G Leffers Jr., PhD whose telephone number is (703) 308-6232. The examiner can normally be reached on 9:30am-6:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel can be reached on (703) 305-1998. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

 Gerald G Leffers Jr., PhD  
Primary Examiner  
Art Unit 1636  
**GERRY LEFFERS**  
**PRIMARY EXAMINER**

Ggl